UNITED STATES DISTRICT COURT

DISTRICT OF NEW JERSEY

APTALIS PHARMA US, INC. and APTALIS PHARMA CANADA ULC, Plaintiffs, vs. PHARMACEUTICAL SOURCING PARTNERS, INC., Defendant.	Civil Action No. 15-8637 (MLC)(LHG)

DECLARATION OF LOYD V. ALLEN, JR., Ph.D., R.Ph.

I, Loyd V. Allen, Jr., Ph.D., R.Ph., submit this declaration in support of the Opening Claim Construction Brief of Plaintiffs Aptalis Pharma US, Inc. and Aptalis Pharma Canada ULC (collectively, "Aptalis").

I. Introduction.

1. I have been retained by Aptalis to provide expert opinions and testimony in the above-captioned case. In this declaration, I comment on general matters relating to suppository formulations and their ingredients, and offer opinions on the meaning of certain claim terms of U.S. Patent Nos. 7,541,384 ("the '384 patent"), 8,217,083 ("the '083 patent") and 8,436,051 ("the '051 patent") (collectively, the "Asserted Patents"[1]) in view of my knowledge of the relevant science and technology, the level of knowledge existing during relevant time periods, and the claims, specifications, and prosecution histories of the Asserted Patents.

2. In forming my opinions, I have reviewed the Asserted Patents, their prosecution histories, the parties' proposed claim constructions, and other materials discussed

[1] The Asserted Patents are Attached to the September 23, 2016 Declaration of Charles H. Chevalier ("Chevalier Decl.") as Ex. 1 ('384 Patent), Ex. 2 ('083 Patent) and Ex. 3 ('051 Patent). Throughout this declaration, all references to exhibits 1-20 shall refer to the attachments to the Chevalier Declaration.

in this declaration. In reaching my conclusions, I have also drawn upon my years of education, training, and experience in the pharmaceutical field.

3. This declaration sets forth observations, opinions, and conclusions that I hold today. These observations, opinions, and conclusions are based on information currently available to me. I reserve the right to amend, supplement, and/or modify my opinions as new issues arise or as new information becomes available to me as the case progresses. I further reserve the right to form additional opinions upon hearing new information, and/or to offer additional rebuttal testimony to any evidence or argument advanced by defendant Pharmaceutical Sourcing Partners, Inc. ("PSP").

II. Educational and Professional Background.

4. I am Chair and Professor Emeritus of the University Of Oklahoma College Of Pharmacy, Department of Medicinal Chemistry and Pharmaceutics; Editor-in-Chief of the International Journal of Pharmaceutical Compounding; Editor-in-Chief of *Remington: The Science and Practice of Pharmacy*; and CEO of the Midwest Institute of Research and Technology (a pharmaceutical consulting and contract research organization). My educational background, professional experience, and qualifications are set forth in my curriculum vitae, which is attached as Exhibit ("Ex.") A. Below I highlight some aspects of my educational and professional background relevant to this case.

5. I earned my B.S. and M.S. degrees in Pharmacy from the University Of Oklahoma College Of Pharmacy in 1966 and 1970, respectively. I completed a residency in hospital pharmacy at the U.S. Public Health Service Hospital in Boston in 1966-67 and received my Ph.D. in Pharmaceutics from the University of Texas at Austin in 1972. I have been a Registered Pharmacist in Oklahoma since 1966. I was also licensed as a Clinical Laboratory Director from 1978 to 1985.

6. I became an Assistant Professor of Pharmacy at the University of Oklahoma in 1972, and was promoted to Full Professor in 1982. I served as Chair of the Department of Medicinal Chemistry and Pharmaceutics from 1994 to 1998 and have been a Professor Emeritus since 1998. Over the years, I have supervised more than 50 master's students, doctoral students and post-doctoral fellows working in the areas of pharmaceutical formulation, the characterization of suppositories and other drug dosage forms, and the characterization of active pharmaceutical ingredients ("APIs") and excipients. I have also worked on more than a dozen consulting projects involving the formulation and development of a broad range of APIs and dosage forms.

7. For 35 years extending until 2014, I served as a member of numerous committees of the United States Pharmacopeial Convention, the preeminent national pharmaceutical standard-setting organization. For example, I have served on the Committee of Revision (1990-2000), the Expert Advisory Panel on Pharmacy Compounding Practices (1993-2000), the General Policies Executive Committee

(2000-2005), the Nomenclature Committee (2000-2013), and the Executive Committee (2005-2010). From 2000 to 2010, I served as Chair of the Expert Committee on Pharmacy Compounding.

8. I also served on the FDA's Pharmaceutical Compounding Advisory Committee and on National Cancer Institute Study Sections that evaluated grant proposals for innovative drug delivery technologies.

9. I am or have been a member of numerous scientific societies, including, for example: the American Pharmaceutical Association, the Academy of Pharmaceutical Research and Science, the American Society of Health Systems Pharmacists, the American Association of Colleges of Pharmacy, the American Association of Pharmaceutical Scientists (Charter Member), the American College of Apothecaries, the International Academy of Compounding Pharmacists, and the Controlled Release Society.

10. During my career, I have received many honors and awards. For example, in 1998, I received the J. Leon Lascoff Memorial Award, the highest award given by the American College of Apothecaries. I have been named a fellow of the American College of Apothecaries (1995), the Academy of Pharmaceutical Research and Science of the American Pharmaceutical Association (1996), and the International Academy of Compounding Pharmacists (1996).

11. I founded the International Journal of Pharmaceutical Compounding in 1996, and currently serve as its Editor-in-Chief.

12. Since 2011, I have been Editor-in-Chief of *Remington: The Science and Practice of Pharmacy*, which is one of the leading handbooks for pharmacists and pharmaceutical formulators.

13. I have authored 87 experimental publications in peer-reviewed scientific journals, 115 experimental abstracts, 70 book chapters and monographs, and more than 1,000 other professional publications on topics relating to pharmaceutical formulations, API characterization, dosage forms (including more than 30 publications on suppositories), pharmaceutical compounding, and compounding calculations.

14. I am the author of "Suppositories," a book published in 2007 that provides a review of suppository dosage forms. It contains chapters covering, among other things, the history and development of suppositories; suppository bases and their characteristics; pharmaceutical, biopharmaceutical and pharmacokinetic factors; and special types of suppositories. I have also authored multiple editions of two textbooks on pharmaceutics and dosage forms. My textbooks have been translated into several foreign languages.

15. I have been granted 13 United States patents in the field of pharmaceutical formulation.

16. I have extensive practical experience measuring the characteristics of pharmaceutical products and their ingredients in accordance with USP industry-standard procedures as required by the claims of the Asserted Patents. For example, I have performed hundreds of tap density tests according to USP <616>, open-capillary tube melting point determinations according to USP <741>, and dissolution tests using USP paddle apparatus #2 according to USP <711>. In addition, I have taught graduate-level pharmacy and pharmaceutics students about USP procedures for measuring the characteristics of pharmaceutical products and their ingredients, including measurements of the surface area of powders in accordance with USP <846>.

17. In summary, over the years, I have acquired substantial experience and expertise in several areas relevant to this litigation, including, without limitation:

- Drug dosage form development, formulation, and testing;
- Development, manufacturing, and testing of suppositories, including quality control and quality assurance tests and procedures;
- Characterization of the physical and chemical properties of APIs and excipients; and
- United States Pharmacopeia ("USP") standards for the identity, strength, quality, and purity of medicines and pharmaceutical ingredients, and USP standard testing techniques for pharmaceutical products and ingredients.

18. In the past four years, I have testified in the following cases:

- *Shire Dev. Inc., et al. v. Cadila Healthcare Ltd. (d/b/a Zydus Cadila), et al.*, Civil Action No. 1:10-cv-00581-LPS;
- *Shire Dev. Inc., et al v. Watson Pharms., Inc., et al.,* Civil Action No. 0:12-60862-CIV;
- *Aptalis Pharma US Inc., et al. v. Sandoz, Inc.*, Civil Action No. 13-cv-4290 (MLC)(LHG);
- *Aptalis Pharma US Inc. et al. v. Mylan Pharmaceuticals Inc. et al.,* Civil Action No. 13-cv-4158 (MLC)(LHG);
- *MEDA AB et al. v. The Minister of Health and Pharmascience Inc. et al.,* Court File No. T-200-15;
- *New England Compounding Pharmacy, Inc. Products Liability Litigation*, MDL No. 2419; Master DKT. 1:13-md-02419-RWZ; and
- *Australia Patents Act 1990 In the Matter of Patent Acceptance 2008320992 in the Name of Bayer B.V. and IN THE MATTER OF Opposition thereto by Merial Limited.*

19. I am being compensated at my standard hourly rate of $400 for my time in this case. My compensation is not dependent upon the outcome of the case.

III. The Level of Ordinary Skill in the Art.

20. I understand that for purposes of interpreting the disputed claim terms, it is necessary to examine those terms from the viewpoint of a person of ordinary skill in the art ("POSA") at the time the patent applications were filed.

21. I have been instructed by counsel to assume that the filing date is June 8, 2007 for the '384 and '083 patents and for those claims of the '051 patent that do not recite a mesalamine surface area property. I have been further instructed to assume that the filing date is December 16, 2009 for those claims of the '051 patent that recite mesalamine surface area properties.

22. In my opinion, the arts relevant to the Asserted Patents are pharmaceutical arts, including the development, formulation, testing, and manufacturing of pharmaceutical dosage forms and characterization of their ingredients (including APIs and excipients) in accordance with USP methods. Formulation of the suppository dosage form presents unique challenges and, therefore, the arts specifically dealing with suppositories would have particular relevance to the Asserted Patents.

23. In my opinion, a POSA at the relevant time would have been someone working in the pharmaceutical arts with knowledge of API testing, the development and testing of pharmaceutical formulations, and processes for manufacturing solid dosage forms such as suppositories. A POSA would have gained this knowledge either through experience working in drug development, formulation and/or manufacturing, or through training (such as a graduate degree in a pharmaceutical science). A POSA would also have several years of work experience or training in one or more of the relevant arts described above.

IV. Background of Pharmaceutical Formulation.

24. In the pharmaceutical arts, the term "dosage form" refers to the combination of a drug substance (API) such as mesalamine with pharmacologically inert ingredients (excipients) such as a hard fat suppository base.

25. One may use many different types of dosage forms to administer a drug to a patient. Common dosage forms include, for example, tablets, solutions, creams, ointments, aerosols, transdermal patches, and suppositories.

26. A single API may be formulated into multiple dosage forms, because different medical conditions can warrant different routes of administration. For example,

mesalamine is a drug useful for treating various inflammatory bowel conditions such as ulcerative colitis and ulcerative proctitis.[2] Mesalamine has been formulated into both oral dosage forms (such as delayed- and extended-release tablets and capsules) and rectal dosage forms (such as suppositories and enemas).[3] Rectal dosage forms are particularly useful for treating colon conditions because they deliver the drug directly to the site of inflammation, thereby avoiding many of the side effects of oral mesalamine drugs.[4]

27. Different dosage forms (even for the same active ingredient) present unique formulation and design challenges. For example, some excipients suitable for oral administration are not suitable for rectal administration. The different timing of drug release as well as the different physiological microenvironments each dosage form is exposed to also impact formulation choices, including selection of the physical and chemical properties of the API, proper excipients, and manufacturing techniques.

V. Background of the Inventions.

28. The Asserted Patents relate to mesalamine rectal suppository drug products and methods of their use. The mesalamine rectal suppositories of the Asserted Patents are characterized by the amount of mesalamine they contain, their drug load,[5] and/or their mesalamine release rate under specified conditions. The claimed suppositories are made from mesalamine and a suppository base characterized by several physical properties, including the tap density and/or surface area of the mesalamine, and/or the ascending melting point of the suppository base. The USP standard methods for measuring these properties of mesalamine suppositories and their ingredients were well known to POSAs, and, as described more fully below, the claim terms reciting these various properties would have been unambiguously understood by POSAs.

VI. The USP Promulgates Industry-Standard Procedures for Measuring Properties of Pharmaceutical Products and Their Ingredients.

29. The United States Pharmacopeial Convention is a nonprofit scientific organization that sets standards for the identity, strength, quality, and purity of medicines manufactured, distributed and consumed worldwide.

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[2] *E.g.*, '384 patent at col. 1; '083 patent at col. 1; '051 patent at col. 1.

[3] *E.g.*, '384 patent at 1:53–2:12; '083 patent at 1:55–2:10; '051 patent at 1:58–2:11.

[4] *Id*.

[5] As agreed by the parties, the term "drug load" is defined in the Asserted Patents and means "the weight percentage of mesalamine based on the total weight of the suppository" (*e.g.*, Joint Claim Construction and Pre-Hearing Statement ("JCCS"), ECF #41 at 2; '384 patent at 4:56-57; '083 patent at 5:4-5; '051 Patent at 8:3-4.

30. The United States Pharmacopeial Convention develops and publishes a book of public pharmacopeial standards called *The United States Pharmacopeia and The National Formulary* ("USP–NF" or just "USP"). The United States Pharmacopeial Convention has been publishing new editions annually since 2002. Chapters in the USP-NF are designated using a standard nomenclature with bracketed numbers. For example, USP-NF Chapter 616 is referred to as USP <616>.

31. The USP-NF contains "monographs" for APIs (in the USP) and excipients (in the NF) that set forth quality and purity standards for pharmaceutical ingredients. If a monograph has been developed for an ingredient (such as mesalamine), that ingredient must meet the standards set forth in that monograph when incorporated into a pharmaceutical product (such as a mesalamine suppository):

> "Official drug products and finished devices are prepared from ingredients that meet the requirements of the compendial monographs for those individual ingredients for which monographs are provided."[6]

32. In the United States, USP standards are enforced by the Food and Drug Administration.[7] The Food, Drug, and Cosmetics Act designates the USP–NF as the official compendia for drugs marketed in the United States. A drug product distributed in the U.S. market must conform to the standards in the USP–NF to avoid possible charges of adulteration and misbranding.[8]

33. The tests and assays described in the USP define mandatory industry standards that POSAs must use to assay pharmaceutical products and their ingredients. As the USP states:

> "[The USP contains] more than 200 *General Tests and Assays* (General Chapters numbered 1,000 and below) and *General Information Chapters* (numbered above 1,000). General Chapters provided frequently cited procedures, sometimes with acceptance criteria, in order to compile into one location repetitive information that appears in many monographs."[9]

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[6] USP 30/NF 25 Introductory Sections, *General Notices and Requirements* at 5, attached as Ex. B to this declaration.

[7] *See, e.g.*, http://www.usp.org/about-usp (last visited on September 16, 2016), Ex. 4.

[8] *See, e.g.*, http://www.usp.org/usp-nf (last visited on September 16, 2016), attached as Ex. C to this declaration.

[9] USP 30-NF 25 Introductory Sections, *Mission and Preface*, Ex. B at v.

The *General Notices* section further states that the assays and tests set forth in the General Chapters "are intended to serve as ***the official test methods*** in the event of a question or dispute as to whether the compounded preparation complies with official standards."[10] Thus, when there is a USP chapter that describes how to measure a particular property of a pharmaceutical product or its ingredients, POSAs working in the pharmaceutical industry would know that they must follow that USP method.

34. The official test methods described in the General Chapters of the USP-NF were developed through an extensive process that ensures they are robust and reliable. Proposals for a new or revised method can come from the pharmaceutical industry, the USP staff, or from a USP expert committee. The method is first validated by the USP staff or an independent laboratory and then published to initiate a 90-day public comment period. The relevant USP expert committee considers comments from the pharmaceutical industry, the FDA, and other interested parties. If the committee approves the method, it becomes official and is incorporated into the next edition of the USP-NF.

35. The specifications of the Asserted Patents make clear that the claimed "mesalamine rectal suppository" and its ingredients should satisfy USP-NF requirements and that the properties of the claimed suppositories and their ingredients should be measured using the methods set forth in the USP. Indeed, the USP is incorporated by reference into the Asserted Patents, which cite "The United States Pharmacopeia" and state that "[a]ll non-patent references … cited and discussed in this specification are incorporated herein by reference in their entirety and to the same extent as if each was individually incorporated by reference."[11]

36. Additionally, the specifications of the Asserted Patents discuss the inventions in the context of improvements over CANASA® mesalamine suppositories.[12] CANASA® is an FDA-approved product, so one must test CANASA® suppositories and their ingredients according to USP methods. Therefore, a POSA would have understood that the claimed mesalamine rectal suppositories and their ingredients (like CANASA® and its ingredients) must also be tested using the relevant USP methods. Indeed, the claims and specifications of the Asserted Patents repeatedly refer to the USP and National Formulary (or NF) when describing the ingredients of the claimed suppositories and methods for testing suppositories and their ingredients. This would further indicate to POSAs that USP-NF quality standards and testing procedures apply.

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[10] USP 30/NF 25 Introductory Sections, *General Notices and Requirements*, Ex. B at 6 (emphasis added).

[11] *E.g.*, '384 patent 14:6-9; '083 patent at 14:5-8; '051 patent at 19:39-42.

[12] *E.g.*, '384 patent at 2:8-12; '083 patent at 2:5-10; '051 patent at 2:7-11.

37. Different versions of the USP were in effect on the different filing dates of the Asserted Patents.[13] Nevertheless, the USP General Chapters and Monographs relevant to this dispute were substantially the same. In fact, many USP Chapters and Monographs had been in effect for years without substantial modification and thus, had long-standing acceptance as U.S. pharmaceutical industry standards.

38. I was a member of the USP Council of Experts and the Council of Experts Executive Committee from 2000 to 2008 and helped oversee the development of the USP standards for all dates relevant to this dispute.[14]

39. USP 30/NF 25 (and several editions before, and each edition thereafter) contains monographs relating to mesalamine and hard fat.[15] Mesalamine that meets USP-NF standards is labeled as "mesalamine, USP" or "mesalamine (USP)." The specifications of the Asserted Patents use the "mesalamine (USP)" and "mesalamine powder USP" notations.[16] Similarly, hard fat that meets USP-NF standards is referred to as "hard fat NF" and this is the notation the Asserted Patents use to refer to hard fat.[17] A POSA would have understood the "mesalamine (USP)" and "hard fat NF" notations in the Asserted Patents to indicate that USP-NF quality standards are applicable to the mesalamine and hard fat ingredients of the claimed suppositories and that one should use USP testing methods when testing the claimed suppositories and their ingredients.

40. USP 30/NF 25 and USP 32/NF 27 contain substantially identical versions of USP General Chapter <616>. This chapter provides the U.S. pharmaceutical industry-standard procedure for measuring the ***tap density*** of pharmaceutical powders.[18] Tap density is the density of a powder after it has been placed in a container and repeatedly tapped to reduce the volume of empty space between particles of the powder. When formulating a pharmaceutical product from a particulate ingredient such as mesalamine that is required to have a particular tap density, a POSA would have measured tap density using a technique described in USP <616>.

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[13] USP 30/NF 25, which was published in November 2006 and was "official" from May 2007 until May 2008, was the official USP edition on the effective filing date of the '384 and '083 patents and for the Asserted Claims of the '051 patent that do not recite mesalamine surface area (1-18, 26, and 45-47). USP 32/NF 27 was the official edition on the 2009 filing date for the remaining claims of the '051 patent. In addition, the patents cite USP 23/NF 18 (from 2000). *E.g.*, '384 patent at 5:30-31; '083 patent at 5:46-47; '051 patent at 8:48-49. The "30" in "USP 30" indicates that this is the 30th edition of the USP; the "NF 25" refers to the 25th edition of the National Formulary, which has been published with the USP since the 1970s.

[14] USP 30-NF 25 Introductory Sections *People*, Ex. B at xi-xvi.

[15] *E.g.,* Mesalamine, USP, Ex. 5; Hard Fat, NF, Ex. 6.

[16] *E.g.*, '384 patent at 7:44 & 13:45; '083 patent at 7:57 & 13:45; '051 patent at 1:9 & 17:17.

[17] *E.g.*, '384 patent at 2:41-42; '083 patent at 2:45; '051 patent at 2:56.

[18] USP <616>, Ex. 7.

41. USP 30/NF 25 and USP 32/NF 27 contain substantially identical versions of USP General Chapter <711>. This chapter provides the U.S. pharmaceutical industry-standard procedures for measuring the ***dissolution of and release of API*** from pharmaceutical dosage forms.[19] When testing a pharmaceutical dosage form such as a mesalamine suppository that is required to have a particular release rate, a POSA would have used a technique described in USP <711>.[20]

42. USP 30/NF 25 and USP 32/NF 27 contain substantially identical versions of USP General Chapter <741>. This chapter provides the U.S. pharmaceutical industry-standard procedure for measuring the ***ascending melting point*** of ingredients.[21] The ascending melting point is the temperature at which an ingredient begins to transition from a solid to a liquid as the temperature rises. When measuring the ascending melting point of a suppository base, a POSA would have used a technique described in USP <741>.

43. USP 30/NF 25 and USP 32/NF 27 contain substantially identical versions of USP General Chapter <846>. This chapter provides the U.S. pharmaceutical industry-standard procedure for measuring the ***specific surface area*** of a powder.[22] When formulating a pharmaceutical product from a particulate ingredient (such as mesalamine) that is required to have a particular surface area, expressed per unit weight (*i.e.*, specific surface area), a POSA would have used a technique described in USP Chapter <846>.

44. In summary, a POSA would have understood that the physical properties claimed in the '384, '083 and '051 patents (*e.g.*, mesalamine tap density, mesalamine surface area, hard fat ascending melting point, and suppository mesalamine release rate) should be measured according to the industry-standard techniques described in the relevant USP Chapter. In part, a POSA would use USP methods because the USP is referred to repeatedly throughout the specifications and claims of the Asserted Patents and was incorporated by reference into the Asserted Patents. But, even if the Asserted Patents never mentioned the USP, a POSA would have understood the invention to relate to pharmaceutical formulations and drug substances for human use, and would therefore have known that the USP's industry standards must apply.

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[19] USP <711>, Ex. 8.

[20] As described more fully below, the general techniques described in USP Chapter <711> are made specific for a particular dosage form and/or active ingredient by specifying other properties such as the buffer, pH, temperature and mixing speed. These properties may be specified in the particular monograph for the dosage form in the USP, or may be specified by the FDA or an individual researcher. As described more fully below, and as evident from the claim language itself, the claims of the '384, '083 and '051 patents provide all of the specific parameters necessary to test the dissolution of mesalamine rectal suppositories in accordance with the claimed inventions.

[21] USP <741>, Ex. 9.

[22] USP <846>, Ex. 10.

45. As detailed below, the relevant USP Chapters provide specific step-by-step instructions and test conditions required to measure the claimed properties of mesalamine suppositories and their ingredients.

VII. Construction of Disputed Terms.

46. I understand that the parties dispute 17 claim terms (and their minor variations). However, because construction of many of these terms involves the same general issues, they should be construed together as discussed below. Additionally, I believe that identical claim terms should be given identical constructions in all claims of the three Asserted Patents. I see no basis in the specifications or prosecution histories of the Asserted Patents to construe identical terms differently.

A. Construction of "About."

47. As discussed above, the inventions claimed in the Asserted Patents relate to specific properties of suppositories and their ingredients. Some of these properties, including the amount of mesalamine, drug load, release rate, tap density, and surface area are claimed as values or ranges modified with the word "about." In the pharmaceutical field, a POSA would have understood the word "about" to have its ordinary meaning of "approximately." I find no evidence in the specifications or prosecution histories of the Asserted Patents that the inventors intended that "about" should have a different meaning.

B. Construction of "Mesalamine Particles."

48. I believe the phrase "mesalamine particles" does not require a construction. A POSA would have understood this phrase to have a plain and ordinary meaning and to refer to mesalamine in powder form (or simply mesalamine).

49. As discussed above, the claimed mesalamine rectal suppositories comprise mesalamine. The specifications of the Asserted Patents make clear that the mesalamine used to prepare the claimed suppositories is in a powder form. For example, in describing how to manufacture the claimed mesalamine suppositories, the specifications state "[t]he mesalamine (e.g., in ***powder form***) is typically dispersed in a suppository base, such as hard fat."[23] In describing the manufacture of suppositories, the specifications similarly state:

> "Slowly add 100.0 kg of ***mesalamine powder*** USP to the mix tank. During the addition of the ***powder***, slowly increase the sweeps to 35 Hz and the prop to 35 Hz as the product level in the tank increases, minimizing aeration. The addition of the ***powder*** must be performed

[23] *E.g.*, '384 patent at 5:21-22; '083 patent at 5:37-38; '051 patent at 8:39-40 (emphasis added); *see also* '384 patent at 6:31-32; '083 patent at 6:48-49; '051 patent at 8:64-65 ("mesalamine is preferably in the form of a ***powder*** of unagglomerated needle-shape crystals.")(emphasis added).

> over a 35 to 60 minute interval. The ***powder*** must be completely dispersed prior to mixing."[24]

50. Accordingly, I believe the specifications of the Asserted Patents use the terms "mesalamine powder" and "mesalamine" interchangeably.

51. The plain meaning of the term "powder" is "a substance composed of finely dispersed solid particles."[25] Indeed, the '051 patent defines mesalamine and mesalamine powder as comprising particles or "crystals":

> "The term 'mesalamine' refers to 5-aminosalicylic acid (5-ASA). According to one embodiment, the mesalamine has the following particle size distribution: X10 of about 5 to about 11 μm, X50 of about 25 to about 45 μm, and X90 of about 85 to about 100 μm."[26]
>
> "Preferably, the mesalamine is not in the form of granules suitable for compaction into tablets. Rather, the ***mesalamine is preferably*** in the form of a ***powder of unagglomerated*** needle-shape ***crystals.***"[27]

52. Thus, a POSA would have understood that the term "mesalamine particles" refers to mesalamine supplied in the form of a powder, which consists of particles. Accordingly, the term "mesalamine particles," as used in the specifications and claims of the Asserted Patents, does not require a construction different from its plain and ordinary meaning.

C. Construction of the Suppository Base Terms.

1. Construction of "an oily or fatty base."

53. A POSA would have understood the claim term "an oily or fatty base" to mean "*a base that can be oily, fatty or both*."

54. The specifications of the Asserted Patents discuss only a ***single*** class of hydrophobic bases, not two separate classes of bases.[28] This single class of bases (referred to in the specifications as "oily or fatty") includes bases such as hard ***fat*** and theobroma ***oil***.[29] The conjunctive use of "or" in "oily or fatty base" as two synonymous

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[24] *E.g.*, '384 patent at 7:44-45; '083 patent at 7:57-58; '051 patent at 11:9-10 (emphasis added).

[25] Webster's II New College Dictionary, Houghton Mifflin, 2001 ("Websters"), attached as Ex. D to this declaration.

[26] '051 patent at 7:65-8:2.

[27] '051 patent at 9:62-65.

[28] *E.g.*, '384 patent at 5:20-46; '083 patent at 5:37-61; '051 patent at 8:37-65.

[29] *Id*.

descriptors for the same class of bases (*i.e.*, hydrophobic bases) is further supported by a dictionary definition. One of the accepted definitions for "or" is "a synonymous or equivalent expression."[30]

55. Indeed, a POSA would have understood the term "an oily or fatty base" to refer to the hydrophobic (*i.e.*, repelling water) class of suppository bases as opposed to hydrophilic (*i.e.*, having a strong affinity for water) bases. Within the context of the invention, "oily" and "fatty" simply refer to the state of the hydrophobic base, which can be described as "oily" or "fatty" or both oily (at high temperature) and fatty (at low temperature). Hydrophobic suppository bases are required to be solid at room temperature (*i.e.*, fatty) so they can be packaged, shipped and inserted into the rectum, and then are required to melt (*i.e.*, become oily) once exposed to body temperature so the drug is released from the base.[31] Recitation of "an oily or fatty base" simply expresses this requirement that the base be capable of existing as a fat (*i.e.*, as a solid) or as an oil (*i.e.*, as a liquid), depending on temperature.

56. Aptalis's construction of "oily or fatty base" is also consistent with the understanding of POSAs as reflected in USP industry standards and the pharmaceutical literature. For example, *Remington* describes only three classes of suppository bases: "Cocoa Butter and other Fatty Bases," "Water-Soluble or Dispersible Suppository Bases," and "Hydrogel" bases. Only the "Fatty Bases" are described as oily or fatty. *Remington* states that the most common "***Fatty*** Base" is "Theobroma ***Oil***," demonstrating that POSAs use the terms interchangeably to refer to the same class of bases.[32] *Remington* further states that "Suppositories are ***solid*** dosage forms of various weights and shapes, usually medicated, for insertion into the rectum … After insertion, suppositories ***soften, melt***, disperse or dissolve in the cavity fluids."[33]

57. Similarly, the Dosage Forms section of the USP describes "Cocoa Butter Substitutes" for suppository bases as, "produced from a variety of vegetable ***oils*** … (e.g., ***Hydrogenated Vegetable Oil and Hard Fat***)," indicating that the same class of bases is referred to as an oil and a fat (*i.e.*, oily or fatty).[34]

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[30] Webster's, Ex. D at Definition 2 for "or".

[31] The Asserted Patents confirm this. *E.g.*, '384 patent at 5:60-61; '083 patent at 6:9-10; '051 patent at 9:15-16 ("The melting point of the suppository is generally sufficient to melt in the patient's body").

[32] L.H. Block, *Medicated Topicals* in *Remington: The Science and Practice of Pharmacy* ("Block"), Ex. 11 at 10707-10708.

[33] *Id.* at 10706.

[34] USP <1151>, Ex. 12 at 1473 (emphasis added).

2. Construction of "hard fat."

58. A POSA would have understood the claim term "hard fat" to have its plain and ordinary meaning.

59. The term "hard fat" is a well-accepted and well-understood term in the pharmaceutical industry. The USP has a monograph entitled "Hard Fat," which describes a general composition of hard fat, a standard procedure for measuring the melting range of hard fat as well as standard packaging and labeling procedures.[35]

60. A POSA would understand, in the context of a pharmaceutical composition, that the term "hard fat" refers to an ingredient that satisfies the requirements of the USP *Hard Fat* monograph. For example, in describing suppository ingredients, USP<1151> refers to hard fats as suitable suppository bases without providing any further definition or explanation.[36]

61. The Asserted Patents use the term "hard fat" consistent with its plain and ordinary meaning. For example, the specifications note that "[t]he mesalamine suppository may further include a suppository base, such as ***hard fat*** (e.g., hard fat NF)."[37] A POSA reading the notation "hard fat NF" would have understood that the specifications refer to the USP-NF monograph entitled "Hard Fat" and would have understood that the term "hard fat" has its plain and ordinary meaning. The specifications further confirm that "hard fat" is used in the Asserted Patents consistent with its plain meaning by using it to refer to commercial products:

> "A preferred low melting suppository base is ***hard fat*** having an ascending melting point of 32 to 33.5° C. (e.g., Witepsol® H 12 available from Sasol Germany GmbH of Witten, Germany[38]). Another suitable low melting suppository base is ***hard fat*** having an ascending melting point of 33.5 to 35.5° C. (e.g., Witepsol® H-15 available from Sasol Germany GmbH)."[39]

62. Therefore, the term "hard fat" should be interpreted according to its plain and ordinary meaning: "*hard fat*."

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[35] USP Hard Fat monograph, Ex. 6 at 1438.

[36] USP<1151>, Ex. 12 at 1472 ("Cocoa butter and its substitutes (e.g., *Hard Fat*) perform better than other [suppository] bases…").

[37] *See, e.g.*, '384 patent at 2:41-42; 083 patent at 2:44-45; '051 patent at 2:55-56.

[38] Sasol Germany GmbH sold the WITEPSOL® product line and its production site in Witten, Germany to CREMER OLEO GmbH & Co. KG on January 10, 2012. (http://www.sasol.com/de/media-centre/media-releases/sasol-germany-sell-its-german-production-site-witten-cremer.)

[39] *See, e.g.*, '384 patent at 2:60-66; '083 patent at 3:7-14; '051 patent at 3:33-39.

D. Construction of "moulded suppository."

63. A POSA would have understood the claim term "moulded suppository" to mean "a suppository made in a mould."

64. A POSA would know that one can prepare suppositories by rolling (hand-shaping), molding, or cold compression.[40] The molding process utilizes a hollow container or shell called a "mould" (or "mold" as the word is spelled in the United States). The mold holds a melted preparation containing an active ingredient and a suppository base for a sufficient time to permit solidification of the suppository.[41] After the suppository solidifies, the mold is either broken or separated, permitting the suppository to be extracted for subsequent wrapping and packaging.[42] Suppository molds can be made from a wide range of materials, including, for example, aluminum, plastic, brass, and rubber.[43] Additionally, disposable plastic molds can be used in pharmaceutical manufacturing. These disposable molds not only shape the suppository but also provide a packaging container. [44]

65. Reading the specifications of the Asserted Patents, a POSA would have understood that one would make the claimed moulded mesalamine suppository by molding (or moulding). As explained in the Asserted Patents, the preparation of mesalamine suppositories involves "(A) melting the suppository base, e.g., to form a molten solution, (B) adding mesalamine to the melted suppository base, and (C) ***molding the mixture***."[45] A POSA also would have understood that the molding process is carried out in molds. Indeed, the Asserted Patents expressly state that molds should be used to make the claimed suppositories:

> "The mesalamine suppository of the present invention may be prepared as follows. The mesalamine is dispersed in a suppository base in molten form, which is then ***poured into a suitable mould***, such as a PVC, polyethylene, or aluminum mould."[46]

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[40] *See, e.g.*, Block, Ex. 11 at 10708.

[41] *See, e.g.*, U.S. Patent No 3,104,665 (" '665 patent") at 1:23-26, Ex. 13.

[42] *See, e.g.*, *id*. at 1:26-29.

[43] *See, e.g.*, J. Moini, *Laboratory Procedures for Pharmacy Technicians*, Ex. 14 at 1583-84; Block, Ex. 11 at 10708.

[44] *See, e.g.*,'665 patent, Ex. 13 at 1:44-46; *see also,* The Compounding Lab, University of North Carolina, *All About Suppository Molds and Packaging* (Archived Dec 11, 2008), Ex. 15 at 1590.

[45] *See, e.g.*, '384 patent at 4:20-23; 083 patent at 4:35-38; '051 patent at 5:49-52.

[46] *See, e.g.,* '384 patent at 5:66-69; 083 patent at 6:15-18; '051 patent at 9:21-24 (emphasis added).

66. Therefore, the specification supports interpretation of the term "moulded suppository" as "a suppository made in a mould." I did not find anything inconsistent with this interpretation in the specifications or prosecution histories of the Asserted Patents.

E. Construction of the Claim Terms Reciting Amounts of Mesalamine and Mesalamine Particles.

1. Amount of Mesalamine.

67. The claims of the Asserted Patents have several similar terms reciting amounts of mesalamine contained in the claimed suppositories:

- "from about [X] to about [Y] mg [of] mesalamine";
- "the amount of mesalamine ranges from about 950 to about 1050 mg"; and
- "about 1 g mesalamine."

68. In my opinion, it is logical to consider these terms together because PSP has raised the same claim construction issue for all of these terms—how to interpret the word "about." As discussed above, in my view, a POSA would have interpreted "about" in accordance with its plain and ordinary meaning—"approximately."[47]

69. Accordingly, the amount of mesalamine terms recited above should be interpreted in accordance with their plain and ordinary meaning as follows:

Claim term	Construction
"from about [X] to about [Y] mg [of] mesalamine"	Plain and ordinary meaning: "from approximately [X] to approximately [Y] mg [of] mesalamine"
"the amount of mesalamine ranges from about 950 to about 1050 mg"	Plain and ordinary meaning: "the amount of mesalamine ranges from approximately 950 to approximately 1050 mg"
"about 1 g mesalamine"	Plain and ordinary meaning: "approximately 1 g mesalamine"

[47] *See, supra,* Section VII.A.

70. I did not find anything in the specifications or prosecution histories of the Asserted Patents requiring a different interpretation of these terms.

2. Amount of Mesalamine Particles.

71. Two of the Amount of Mesalamine claims recite "from 1.1 to 2.5 g mesalamine particles." As discussed above, a POSA would have understood the term "mesalamine particles" to have its plain and ordinary meaning and to refer to mesalamine in powder form. Thus, in my opinion, the term "from 1.1 to 2.5 g mesalamine particles" should be given its plain and ordinary meaning (*i.e.*, "*from 1.1 to 2.5 g mesalamine particles*"). I did not find anything in the specifications or prosecution histories of the Asserted Patents requiring a different interpretation of these terms.

F. Construction of the Tap Density Terms.

72. Some of Aptalis's asserted claims specify a "tap density" range for the mesalamine powder used to make the claimed mesalamine suppositories. "Tap density" is a property of a pharmaceutical powder, and refers to "an increased bulk density achieved by mechanically tapping a measuring cylinder containing a powder sample."[48]

73. Tap density claim terms appear in two forms—one reciting a tap density range for "mesalamine," and the other reciting a tap density range for "mesalamine particles":

- "the mesalamine has a tap density ranging from about 600 to about 800 g/L (as measured by USP <616>)"
- "the mesalamine particles have … a tap density ranging from about 600 to about 800 g/L (as measured by USP <616>)"

74. In my opinion, it is logical to consider these terms together because the claim construction issues are the same:

- Both terms require the tap density to be measured as described in USP<616>;
- Both terms recite the same tap density range "from about 600 to about 800 g/L"; and
- As discussed above, both "mesalamine" and "mesalamine particles" have the same meaning—mesalamine in a powder form.

[48] *See, e.g.*, USP <616>, Ex. 7 at 1412.

75. The recited tap density range is modified by the word "about." As discussed above, in my view, a POSA would have understood "about" to have its plain and ordinary meaning of "approximately."[49]

76. A POSA would have also understood that mesalamine powder is ***the starting*** material for making mesalamine suppositories and its tap density should be determined before it is mixed with the suppository base and processed to form a suppository.

77. First, the claim language makes clear that tap density is the property of the mesalamine ingredient itself by reciting that the "mesalamine has a tap density…" Furthermore, the Asserted Patents expressly state that "[t]he tap density of the mesalamine used to prepare the molten mesalamine dispersion is also preferably monitored ***before*** production [of mesalamine suppositories] to ensure that the tap density of the mesalamine is at least about 600 g/L and preferably from about 600 to about 800 g/L." [50]

78. Additionally, USP<616> describes a procedure for measuring the tap density of "powders." [51] The method cannot be performed unless the sample is in a powder form and, thus, cannot be performed on suppositories. This also confirms that the tap density recited in the claims refers to the tap density of the mesalamine ***itself*** before it is incorporated into suppositories.

79. Thus, I believe that the tap density terms should be construed as follows: *"the mesalamine itself [mesalamine particles themselves] has [have …] a tap density ranging from approximately 600 g/L to approximately 800 g/L as measured by USP <616>."*

80. PSP appears to argue that a POSA would not have known how to measure the claimed tap density of mesalamine. I disagree.

81. USP <616>, which the claims expressly recite, provides precise step-by-step instructions for performing tap density measurements:

    1. Measure the weight of a test sample.
    2. Measure the initial volume of the test sample.
    3. Tap the material by raising it and letting it fall a certain number of times.
    4. Measure the compacted volume.
    5. Repeat the tapping procedure until the volume does not change by more than 2%.

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[49] *See, supra,* Section VII.A.

[50] *E.g.,* '384 Patent at 6:25-29; '083 Patent at 6:42-46; '051 Patent at 9:49-54 (emphasis added).

[51] USP <616>, Ex. 7 at 1414 ("Tapped density is achieved by mechanically tapping a measuring cylinder containing a ***powder sample***.") (emphasis added).

6. Calculate the tap density by dividing the weight by the final volume.[52]

82. Accordingly, a POSA would have known how to conduct tap density testing in accordance with USP<616> as the claims of Asserted Patents require.

G. Construction of the Release Rate Terms.

83. The asserted claims of the '384, '083, and '051 patents require the claimed mesalamine suppositories to release a specified amount of mesalamine within or after a certain time under specified measurement conditions. For example, claim 1 of the '384 patent recites:

> "… the suppository **releases at least 75%** by weight of the mesalamine **within 2 hours** of dissolution ***[release rate]***
>
> **"as measured with** USP Apparatus #2 at 40° C., a paddle rotation speed of 125 rpm, and 3 sinker turns in 0.2 M phosphate buffer at a pH of 7.5 ***[release rate measurement conditions]***."

84. The parties dispute the construction of four release rate terms. The four terms should be considered together because the claim construction issues for these terms are the same:

- All release rate terms recite the same release rate measurement conditions.
- The release rate terms require the measurement of the release "within" or "after" the recited time interval.
- Several release rate terms recite numeric ranges modified with "about."

85. To simplify the discussion, I will first address how a POSA would have interpreted the recited release rate measurement conditions, the time for measuring dissolution, and the meaning of "about" in the context of measuring a release rate. I will then explain Aptalis's constructions for the four different styles of the release rate terms.

[52] *Id*. at 1415.

1. General Principles for the Construction of the Release Rate Terms.

a) Construction of the release rate measurement conditions.

86. All four of the disputed release rate terms recite the same measurement conditions: "the suppository releases … mesalamine … as measured with USP Apparatus #2 at 40° C, a paddle rotation speed of 125 rpm, and 3 sinker turns in 0.2 M phosphate buffer at a pH of 7.5." A POSA would have understood this language to have its plain and ordinary meaning.

87. PSP agreed that the measurement conditions claim language does not require a construction.[53] Nevertheless, PSP appears to argue that the measurement conditions language makes every release rate term indefinite because, allegedly, the Asserted Patents do not provide the buffer volume, sinker information, methods and parameters for conducting the test and measuring release, and the time for measurement.[54] I disagree.

88. A POSA would have known that dissolution testing of pharmaceutical dosage forms should be performed according to the general procedures set forth in USP <711>, the USP general chapter titled "Dissolution."[55] Indeed, the claims themselves recite "USP Apparatus #2," which a POSA would have understood as an express reference to a dissolution apparatus described in USP <711>.

89. Moreover, the specifications of the Asserted Patents expressly state that the release rate testing of mesalamine suppositories should be "as described in USP 711 (30th Ed.), the section entitled 'immediate-release dosage forms'."[56] Because the USP did not have a specific release protocol for suppositories at the time of Aptalis's inventions, a POSA would have understood this language to direct him or her to follow the step-by-step testing procedure provided in the section "PROCEDURE/Apparatus 1 and 2/IMMEDIATE-RELEASE DOSAGE FORMS" of USP<711>, as modified by the specific conditions expressly recited in the claims and stated in the specifications.[57] Specifically, a POSA would have been directed by the claim language to conduct release rate tests of suppositories using "USP Apparatus #2 at 40° C," using a "rotation speed of 125 rpm," and using "3 sinker turns in 0.2 M phosphate buffer at a pH of 7.5."

90. Contrary to PSP's assertions, the claims and the specifications (through their incorporation of USP <711>) provide all the information a POSA would need to

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[53] JCCS at 7-11.

[54] *Id*.

[55] USP <711>, Ex. 8.

[56] *E.g.*, '384 patent at 3:66-67; '083 patent at 4:14-15; '051 patent at 5:21-22.

[57] USP <711>, Ex. 8 at 1423.

accurately measure the rate of release of the mesalamine active ingredient. In particular:

- A POSA would have understood (without the need for an express statement) that release rate testing should be performed with a buffer volume of 900 mL. Indeed, the 1 L apparatus capacity was the only vessel capacity universally accepted in 2007.[58] It was customary to ***use a 900 mL buffer volume with the 1 L vessel.*** The customary use of a 900 mL buffer volume is confirmed by additional sources. For example, the FDA database "Dissolution Methods," which was available as of January 30, 2006, shows that a buffer volume of 900 mL should be used to test the release rate of mesalamine suppositories.[59] A POSA would have been familiar with the FDA's dissolution method database and would have understood that its procedures should be followed, given that the invention relates to an improvement over an FDA-approved product—CANASA® mesalamine suppositories.[60] The typical usage of 900 mL as the standard buffer volume for dissolution testing is further confirmed in scientific literature.[61]

- USP <711> indicates where to place the suppository in the apparatus: "The dosage unit is allowed to sink to the bottom of the vessel before rotation of the blade is started."[62]

- USP <711> indicates the type of sinker to use: "A small, loose piece of nonreactive material such as not more than a few turns of a wire helix."[63] The patent specifications confirm that the sinker should be "lightly coiled around the suppository … with only 3 turns of wire helix."[64]

- USP <711> instructs that "test specimens are filtered immediately upon sampling… Use an inert filter that does not cause adsorption of the active ingredient or contain extractable substances that would interfere with the

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[58] *Id*.

[59] FDA "Dissolution Methods" Database, http://www.accessdata.fda.gov/scripts/cder/dissolution/dsp_SearchResults.cfm (last visited June 3, 2016), Ex. 16 at 1477.

[60] *E.g.*, '384 patent at 2:8-12; '083 patent at 2:5-9; '051 patent at 2:7-11.

[61] *See, e.g.*, P. Armenante & F. Muzzio, *Inherent Method Variability in Dissolution Testing: The Effect of Hydrodynamics in the USP II Apparatus* P010418-10438 at 3, Ex. 17 (describing a "900 mL fill level" as part of the "typical operating conditions mandated by the dissolution test procedure" for "standard USP Apparatus II.")

[62] USP <711>, Ex. 8 at 1419-20.

[63] *Id*. at 1420.

[64] *See* claim 1 of the '384, '083, and '384 patents.

analysis."[65] This ensures that the hard fat or any other insoluble component does not interfere with the test.

91. A POSA also would have known how to quantify the released mesalamine and to calculate the percentage of mesalamine released. At the time the Asserted Patents were filed, there were multiple well-known methods for measuring mesalamine, and all of them could have produced valid, accurate, and consistent results.[66] High Pressure Liquid Chromatography ("HPLC") with an on-line UV detector is one of the most commonly used quantitative methods in pharmaceutical laboratories.[67] The USP monograph for mesalamine (and its associated dosage forms) suggests using HPLC methods for quantitating mesalamine.[68] While HPLC certainly could have been used, ***any*** quantitative method that had been validated for measuring mesalamine content and calibrated in accordance with well-known techniques would have yielded the same result. Using any accurate mesalamine quantification method, a POSA could have readily measured the amount of mesalamine released from a suppository within a set time period and calculated the percentage of mesalamine released within that time period using simple arithmetic.

b) The time when dissolution should be measured.

92. I understand that PSP argues that a POSA could not have understood the release rate terms reciting a specific percentage of release "***after***" and "***within***" [y] minutes of dissolution because the claim language does not indicate exactly when one is supposed to measure the release percentage. I disagree.

93. A POSA would have understood the words "after" and "within" to have their plain and ordinary meanings and to provide sufficient guidance as to the period of time when the claimed release rate measurements should be made. PSP's alternative constructions of the release rate terms are consistent with this position.[69] For example, PSP's alternative construction of the terms "the suppository releases (a) at least 41.4% (w/w) of the mesalamine ***after*** 20 minutes of dissolution, and (b) at least 62.3% (w/w) of the mesalamine ***after*** 30 minutes of dissolution," is "the

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[65] USP <711>, Ex. 8 at 1423.

[66] *See, e.g.*, M. Gold, Murti, VePuri, and L.H. Block, *Suppository Development and Production* in *Pharmaceutical Dosage Forms: Disperse Systems* ("Gold"), Ex. 18 at p. 482 ("Once the drug substance is separated from the excipient(s), any of the many analytical procedures can be used for quantitation of the drug.").

[67] *See, e.g.*, *id.* ("The use of HPLC in pharmaceutical analysis has become the method of choice. Compared with other methods (GC, UV/Vis, titrations, etc.) the suitability of HPLC … has provided the basis for its popularity with both manufacturing and regulatory agencies.").

[68] Mesalamine, USP, Ex. 5 at 1576-77.

[69] PSP provided alternative constructions for all of the release rate terms (including those reciting the words "after" and "within") "if Court finds term[s] not to be indefinite." JCCS at 7-11.

suppository releases (a) no less than 41.4% (w/w) by weight of the mesalamine **after** 20 minutes of dissolution, and (b) no less than 62.3% (w/w) of the mesalamine **after** 30 minutes of dissolution has passed." [70] Similarly, PSP's alternative construction of the term "the suppository releases at least [X%] by weight of the mesalamine **within** [Y hours/minutes] of dissolution" is "the suppository releases no less than [X]% by weight of the mesalamine ***within*** [Y] of dissolution." [71] Thus, PSP construed both "within" and "after" in accordance with their plain and ordinary meanings and did not find it to be necessary to further clarify the meaning of these terms.

94. In summary, I believe that use of the word "after" in the release rate terms would have indicated to a POSA that mesalamine release should be measured "after" the recited time interval, allowing, for example, for the small amount of additional time it would take to withdraw a sample from the dissolution apparatus. I further believe that use of "within" in the release rate terms would have indicated to a POSA that mesalamine release should be measured "within" the recited time interval (*i.e.*, by the end of the specified time period).

c) The meaning of "about" in the context of measuring release rates.

95. When construing the release rate terms, a POSA would have interpreted "about" in accordance with its plain and ordinary meaning of "approximately" for the same reasons I previously discussed.[72]

2. Constructions for the Release Rate terms.

a) Construction of "the suppository releases at least [X%] by weight of the mesalamine within [Y hours/minutes] of dissolution."[73]

96. Consistent with the principles described above, a POSA would have construed this term in accordance with its plain and ordinary meaning as "*The suppository releases*

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[70] JCCS at 9.

[71] *Id*. at 8-9.

[72] *See, supra,* Section VII.A.

[73] The construction of this generic term applies to the following specific claim terms:

- "the suppository releases at least 75% by weight of the mesalamine within 2 hours of dissolution."
- "the suppository releases at least 80% by weight of the mesalamine within 2 hours of dissolution."
- "the suppository releases at least 80% by weight of the mesalamine within 1 hour of dissolution."
- "the suppository releases at least 90% by weight of the mesalamine within 30 minutes of dissolution."

no less than [X%] by weight of the mesalamine by the end of [Y hours/minutes] of dissolution."

b) Construction of "the suppository releases at least about [X%] by weight of the mesalamine within [Y hour(s)] of dissolution"[74]

97. Consistent with the principles described above, a POSA would have construed this term in accordance with its plain and ordinary meaning as "*The suppository releases approximately [X%] by weight of the mesalamine by the end of [Y hour(s)] of dissolution.*"

c) Construction of "the suppository releases … at least [X%] (w/w) of the mesalamine after [Y] minutes of dissolution."[75]

98. Claims 31 and 33 of the '051 patent recite lower limits for the amount of mesalamine released after a certain time. The parties disagree how these claim terms should be grouped for construction. PSP appears to argue that each numeric term should be interpreted separately.[76] I disagree.

99. The claim construction issues for these terms are the same because the numeric values themselves are not disputed and all of the other words recited in these terms are identical. Thus, all of the release rate terms with the same language in claims 31 and 33 should be construed as a single generic term: "the suppository releases … at least [X%] (w/w) of the mesalamine after [Y] minutes of dissolution." Consistent

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[74] The construction of this generic term applies to the following specific claim terms:

- "the suppository releases at least about 75% by weight of the mesalamine within 2 hours of dissolution."
- "the suppository releases at least about 80% by weight of the mesalamine within 2 hours of dissolution."
- "the suppository releases at least about 80% by weight of the mesalamine within 1 hour of dissolution."
- "the suppository releases at least about 85% by weight of the mesalamine within 1 hour of dissolution."

[75] The construction of this generic term applies to the following specific claim terms:

- "the suppository releases…at least 41.4% (w/w) of the mesalamine after 20 minutes of dissolution."
- "the suppository releases…at least 62.3% (w/w) of the mesalamine after 30 minutes of dissolution."
- "the suppository releases…at least 27.9% (w/w) of the mesalamine after 20 minutes of dissolution."
- "the suppository releases…at least 32.5% (w/w) of the mesalamine after 30 minutes of dissolution."

[76] JCCS at 9 and 10.

with the principles described above, a POSA would have construed this generic term in accordance with its plain and ordinary meaning as *"the suppository releases … no less than [Y%] (w/w) of the mesalamine after [Y] minutes of dissolution."*

d) Construction of "the suppository releases … between [X%] and [Y%] (w/w) of the mesalamine after [Z] minutes of dissolution." [77]

100. Claims 33 and 35 of the '051 patent recite ranges for the amount of mesalamine released after a certain time. The parties disagree how these claim terms should be grouped for construction. PSP appears to argue that each numeric term should be interpreted separately.[78] I disagree.

101. The claim construction issues for these terms are the same because the parties do not dispute the numeric values themselves and all of the other words recited in these terms are identical. Thus, all of the release rate terms with the same language in claims 33 and 35 should be construed as a single generic term: "the suppository releases … between [X%] and [Y%] (w/w) of the mesalamine after [Z minutes] of dissolution." Consistent with the principles described above, a POSA would have construed this generic term in accordance with its plain and ordinary meaning as "*the suppository releases … no less than [X%] and no more than [Y%] (w/w) of the mesalamine after [Z] minutes of dissolution*."

H. Construction of the Ascending Melting Point Term.

102. A POSA would have understood the term "the [oily or] fatty base has an ascending melting point [ranging] from [x] to [y]° C," as used in the context of the Asserted Patents' claims, to mean "*the [oily or] fatty base itself has an ascending melting point [ranging] from [x] to [y]° C."*[79]

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[77] The construction of this generic term applies to the following specific claim terms:

- "the suppository releases between 15.0% and 95.1% (w/w) of the mesalamine after 10 minutes of dissolution."
- "the suppository releases between 19.1% and 40.3% (w/w) of the mesalamine after 10 minutes of dissolution."
- "the suppository releases…between 27.9% and 70.7% (w/w) of the mesalamine after 20 minutes of dissolution."
- "the suppository releases…between 32.5% and 94.8% (w/w) of the mesalamine after 30 minutes of dissolution."

[78] JCCS at 10 and 11.

[79] This generic term applies to the following specific terms:

- "the fatty base has an ascending melting point ranging from 32 to 33.5°C."
- "the fatty base has an ascending melting point from 33 to 35.5°C."
- "the oily or fatty base has an ascending melting point ranging from 33 to 35.5° C."
- "the oily or fatty base has an ascending melting point from 33 to 35.5°C."

103. I believe this term should be construed in accordance with its plain and ordinary meaning, except that it should be clarified that the ascending melting point is a property of the suppository base ***starting*** material. This is why I believe the construction should refer to the "fatty base ***itself***" as stated above.

104. This construction is supported by the express claim language reciting "the ***[oily or] fatty base has*** an ascending melting point…"[80] The specifications of the Asserted Patents further confirm that the ascending melting point is a property of the suppository base itself before it is mixed with any other ingredient. For example, the specifications describe the claimed suppositories as "***prepared from*** … hard fat having an ascending melting point of 32 to 33.5°C (Witepsol® H12) or 33.5 to 35.5°C (Witepsol® H15)."[81]

105. PSP appears to argue that this claim term is indefinite because the Asserted Patents allegedly do not provide a method for measuring ascending melting point.[82] I disagree.

106. First, a POSA does not need to measure ascending melting point to determine whether a suppository base can be used to make the claimed mesalamine suppositories. Suppository bases with the claimed ascending melting point ranges are sold commercially and can be simply ordered from product catalogs, which specify their ascending melting point. Examples of such suitable commercially sold bases are provided in the Asserted Patents. For example, the patent specifications describe "Witepsol® H12 available from Sasol Germany GmbH of Witten, Germany" as having an "ascending melting point of 32 to 33.5°C" and "Witepsol® H15 available from Sasol Germany GmbH of Witten, Germany" as having an "ascending melting point of 33.5 to 35.5°C."[83] The product catalog for "Witepsol® bases for suppositories" has a chart listing values for "Ascending Melting Point [°C]" of Witepsols H12 and H15 that match the values recited in the patents.[84] Thus, a POSA would know that he or she can obtain hard fat that meets the

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- "the oily or fatty base has an ascending melting point ranging from 32 to 33.5°C."
- "the oily or fatty base has an ascending melting point ranging from 33 to 35.5°C."

[80] *See, e.g.*, claims 4-5 of the '384 patent; claims 3-4 of the '083 patent; and claims 3-4 and 24-25 of the '051 patent.

[81] *E.g.*, '384 patent at 4:36-40; '083 patent at col. 4:51-55; '051 patent at 7:21-25.

[82] JCCS at 12.

[83] *E.g.*, '384 patent at 2:60-66; '083 patent at 3:7-14; '051 patent at 3:33-39. Sasol Germany GmbH sold the WITEPSOL® product line and its production site in Witten, Germany to CREMER OLEO GmbH & Co. KG on January 10, 2012. http://www.sasol.com/de/media-centre/media-releases/sasol-germany-sell-its-german-production-site-witten-cremer

[84] *Witepsol: Fatty Bases for Suppositories*, Ex. 19 at 1508.

claimed ascending melting point limitations by simply purchasing it as a stock ingredient from a commercial source.

107. Furthermore, even if a POSA needed to measure the ascending melting point of a suppository base (which he or she would not need to do), he or she would know how to do it. As discussed above, the inventions relate to pharmaceutical products, which must comply with USP requirements, and the USP (including all relevant USP chapters) is incorporated by reference into the Asserted Patents. Thus, a POSA would have known to use the industry-standard USP testing methods. USP <741> describes U.S. pharmaceutical industry-standard procedures for measuring ascending melting point.[85]

108. Furthermore, the USP-NF "Fats and Fixed Oils" and "Hard Fat" monographs explain that the melting temperature of fats and oils and hard fat should be determined according to the procedure for Class II materials described in USP <741>.[86] A POSA would have known to use the USP <741> Class II method to measure the ascending melting point of oily or fatty suppository bases and would have been able to follow its step-by-step procedure.

109. Specifically, according to USP<741>, the method involves drawing the material into a capillary tube and then heating it at a rate of 0.5 to 1.0 per minute. "The temperature at which the material is observed to rise in the capillary tube is the melting temperature."[87] Numerous publications confirm that this capillary-tube method disclosed in USP <741> is the standard procedure for measuring the ascending melting point of suppository bases.[88]

I. Construction of the Drug Load Terms.

110. The parties have agreed that "drug load" should be construed consistent with the definition provided in the specification as "*the weight percentage of mesalamine based on the total weight of the suppository.*"[89] The only disputed claim construction issue relevant to this term is how the recited numerical ranges should be interpreted when modified by "about." However, as I discussed above, a POSA would have interpreted "about" in accordance with its plain and ordinary meaning of "approximately" for all claim terms, including the Drug Load terms.[90]

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[85] USP <741>, Ex. 9.

[86] Hard Fat, NF, Ex. 6 at 1438; USP30 <401> Fats and Fixed Oils, Ex. 20 at 1516.

[87] USP <741>, Ex. 9 at 1428.

[88] *See, e.g.*, Gold, Ex. 18 at p. 476 ("Open capillary tube determination of melting temperature … is most useful for verifying the melting point of excipients used in suppository manufacture.").

[89] JCCS at 12.

[90] *See, supra,* Section VII.A.

111. Therefore, I believe a POSA would have understood the claim term "the mesalamine suppository… wherein the drug load ranges from about [X%] to about [Y%]" to mean: "*the weight percentage of mesalamine in the suppository is no less than approximately [X%] and no greater than approximately [Y%], based on the total weight of the suppository*."

J. Construction of the Surface Area Terms.

112. The surface area terms reciting "[the mesalamine particles have a surface area of]/[the surface area of the mesalamine particles ranges] from about [X] m^2/g to about [Y] m^2/g" should be construed as "*the mesalamine particles themselves have a surface area of from approximately [X m^2/g] to approximately [Y m^2/g].***"**

113. The recited surface area range is modified by "about." As discussed above, a POSA would have interpreted "about" as "approximately" in accordance with its plain and ordinary meaning.[91]

114. As also discussed above, the phrase "mesalamine particles" has the plain and ordinary meaning "*mesalamine particles,*" and refers to particles of mesalamine powder or simply mesalamine.

115. As further discussed above, a POSA would have understood that mesalamine powder is the ***starting material*** for making mesalamine suppositories. Like tap density, the surface area of mesalamine should be determined ***before*** the mesalamine is mixed with the suppository base and processed to form a suppository. First, the claim language makes it clear that surface area is a property of the mesalamine ingredient itself by reciting that the "***mesalamine particles*** have a surface area."[92] Furthermore, the Asserted Patents expressly state that "the surface area of the mesalamine ***used to prepare*** the molten mesalamine dispersion is preferably monitored ***before production*** to ensure that the surface area is in the desired range..."[93] This is why I believe the construction of the Surface Area terms should refer to "mesalamine particles ***themselves***" as stated in the proposed claim construction above.

116. PSP appears to argue that the Surface Area claim terms are indefinite because the Asserted Patents allegedly do not provide a method for measuring the surface area of mesalamine particles.[94] I disagree.

117. As discussed above, a POSA would have known to select a USP method for

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[91] *See, supra,* Section VII.A.

[92] *See, e.g.*, '051 patent, claim 19.

[93] '051 patent at 9:54-61 (emphasis added).

[94] JCCS at 13.

determining the surface area of mesalamine because the invention relates to a pharmaceutical product and the use of USP methods is mandatory for pharmaceutical products in the United States. Additionally, as also discussed above, a POSA would be directed to use a USP method for determining surface area because the USP (and all relevant USP chapters) is incorporated by reference into the Asserted Patents.

118. USP <846> sets forth the official industry-standard method for measuring the surface area of pharmaceutical powders.[95] A POSA would have known that surface area should be measured by the USP <846> method and would have known to follow the step-by-step instructions provided in that USP chapter.

Executed on September 22, 2016 at Edmond, Okla.

I declare under penalty of perjury that the forgoing testimony is true and correct.

Loyd V. Allen, Jr.

[95] USP <846>, Ex. 10.